SUPPORT FOR THE AMENDMENTS

Claims 2 and 3 were previously canceled.

Claim 1 is canceled herein.

Claims 4, 7, 8, 10, 15, and 20-23 are amended herein.

Claims 24-37 are added herein.

The amendment to Claims 4, 7, 8, 10, 15, and 20-23 and the introduction of Claims 24-37 are supported by, for example, original Claims 1-15, paragraph [0013], paragraphs [0017]-[0021], paragraphs [0026]-[0027], and the Examples.

No new matter has been added by the present amendment.

REMARKS

Claims 4-37 are pending in the present application.

At the outset, Applicants wish to thank Examiner Vogel for the helpful and courteous discussion with their undersigned Representative on November 18, 2010. During this discussion various amendments and arguments in traverse of the outstanding rejections were discussed. The content of this discussion is reflected in the following comments. Reconsideration of the outstanding rejections is requested.

The rejection of Claims 4-6 under 35 U.S.C. §112, first paragraph (written description), is obviated in part by amendment and respectfully traversed in part.

In the outstanding Office Action, the Examiner alleges that the invention of Claims 4-6 lacks sufficient written description because "the claims are drawn to a genus of promoter which are recognized by both SigA and SigE as a result of modifying a sequence recognized by SigA, including claims in which a nucleotide sequence having at least 80 or 90% homology to particular segments of sequences in SEQ ID NO: 1 or SEQ ID NO: 2 is the nucleotide sequence promoter recognized by SigA and has the consensus sequence of SigA and/or promoter functions equivalent to those of the consensus sequence." (page 4, last paragraph, of the Office Action mailed September 3, 2010).

On pages 5-6 of the Office Action, the Examiner makes a series of statements about an apparent lack of a disclosed correlation between function and structure of the compounds beyond those specifically disclosed in the specification. The Examiner's allegations center upon the an apparent position that the artisan would be of insufficient level of skill to

understand how a promoter region can contain two consensus recognition sequences for different promoters where each is defined by their respective -35 and -10 sequences.

In order to make the claims more clear, Applicants have amended Claim 4 herein to (a) recite "A promoter region comprising a consensus sequence recognized by SigA and a consensus sequence recognized by SigE to make it clear that the claimed promoter is a region of DNA that may contain at least two distinct promoters and (b) amend the phrase "by modifying ... vicinity thereof:" so as to define the claimed promoter more structurally rather than functionally.

Moreover, Applicants submit that the skilled artisan would readily appreciate the scope and structure of the claimed promoter based on the description in the specification and the state of the art. First, promoters regulated by Sigma factors in *Bacillus* have been well-studied by many researchers for a long time and a lot of promoters and the consensus sequences have been reported. Evidence to this effect is provided with the list consensus sequences of SigA and SigE, including art citations, **submitted herewith**. Based on this state in the art, the skilled artisan would be able to readily identify any consensus sequence recognized by SigA in the genome of *Bacillus* and identify a promoter region including the sig A consensus sequence and being recognized by SigA that is to be modified.

Modification of the nucleotide sequence would be well-known technique in the art. By using any known techniques (such as SOE-PCR as in Example 1). For example, the skilled artisan would insert or substitute with the sigE consensus sequence in the promoter region, with the sigA consensus sequence being maintained, and would obtain the claimed promoter.

Further, with respect to the homology values related to SEQ ID NO: 1 and SEQ ID NO: 2, recited in Claims 4-6, Applicants submit that the skilled artisan would fully

appreciated the scope and nature of modifications permissible. Indeed, most of the sequence defined in SEQ ID NO: 1 and SEQ ID NO: 2 can be variable without affecting the activity (i.e., presenting a sequence recognized by SigA and/or promoter functions equivalent to those of the consensus sequence). The only requirement on the sequence is that the modified sequence contain the respective -35 and -10 regions that are capable of maintaining SigA and SigE binding and activity. In view of the exemplary SigA and SigE sequences provided in the present application coupled with the list submitted herewith clearly establishes that this would be within the skill of the artisan.

Further, with respect to the general knowledge related to promoter technology, Applicants submit herewith the following references:

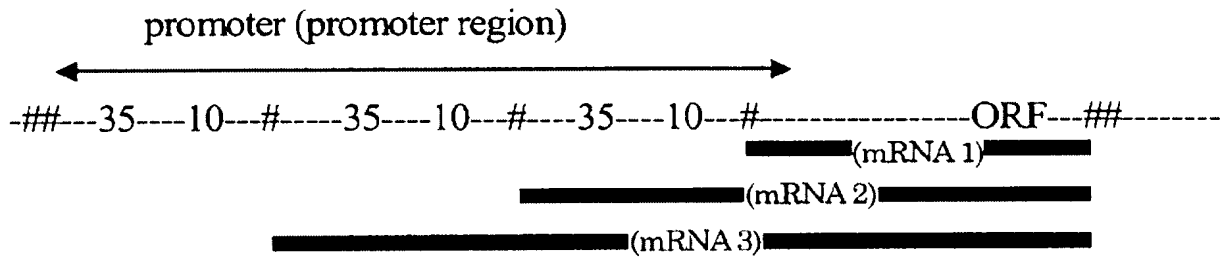
1) Stryer, L. *Biochemistry*: Chapter 29 "RNA Synthesis and Splicing", (1988), pp. 703-732.
2) Hicks and Grossman, *Molecular Microbiology*, (1996), 20(1), 201-212.
3) *Bacillus Subtilis* and Its Closest Relatives: From Genes to Cells, Edited by A. L. Sonenshein, American Society for Microbiology, pp. 289-312, (2002)

Stryer describes the definition of -35 and -10 regions and basic structure of prokaryotic promoter (page 705), function of sigma factor and contribution of sigma factor in gene expression in *Bacillus* (pages 706-707).

Hicks describes that one operon includes promoter region consisting of plural recognition sites by different sigma factors (Introduction and Fig 1).

Sonenshein describes the definition of-35 and -10 regions and basic structure of bacterial promoter (page 290, right column and Figure 1), the consensus sequences of sigma factors (Table 2), and that one operon includes promoter region consisting of plural recognition sites by different sigma factors (page 293, right column and Figure 3).

Stryer and Sonenshein further provide the basic structure of promoter and teach that "-35 region" or "-10 region" is a region in part of promoter, rather than a promoter itself. Hicks and Sonenshein teach that one gene can be regulated by promoter region consisting of plural recognition sites each of which has a -35 region and a -10 region. Therefore, there are plural transcription start sites at the downstream of the plural recognition sites in the promoter region. Because, the -35 region and -10 region are only relative region to transcription start sites. That is, plural mRNA equivalent to the number of recognition sites are made as the result of transcription. Each mRNA length are different, because each length of distance from the each transcription start sites (#) to the terminator (##) of an operon are different (see, below).



Thus, Applicants submit that the skilled artisan would readily appreciate that the SigA and SigE consensus recognition sites are functionally independent to each other irrespective of their location. Applicants further submit that in view of the disclosure in the present specification coupled with the general knowledge in the art, the presently claimed invention complies with the written description requirement of 35 U.S.C. §112, first paragraph.

Withdrawal of this ground of rejection is requested.

The rejection of Claims 1 and 7-23 (and Claims 4-6), under 35 U.S.C. §112, second paragraph, is respectfully traversed.

At the outset, although not acquiescing to the Examiner's allegations, Applicants note that Claim 1 has been canceled. The dependencies of Claims 7-23 has been changed to be based on Claim 4.

In rejecting Claim 4, the Examiner indicates that it is not clear how the "wherein" clauses defining the consensus sequences relates to the claimed promoter. Specifically, the Examiner states that it is unclear how the claim recites a singe promoter containing two separate sequences each of which are promoters. During the discussion with the Examiner on November 18, 2010, the Examiner further explained this concern stating that the use of "promoter DNA" in the preamble is confusing when considering that the language of the claim appears to include features of at least two distinct promoters (one recognized by SigA and one recognized by SigE). Thus, it appears that the Examiner's interpretation is that the claims are using "promoter" to have two different meanings in the claim. To improve clarity of the claims, Applicants have amended Claim 4 recite: "A promoter region comprising a consensus sequence recognized by SigA and a consensus sequence recognized by SigE". Applicants submit that in view of this amendment to Claim 4 in conjunction with the explanation above with respect to the background related to promoters as supported by the references submitted herewith, the claims are definite.

Withdrawal of this ground of rejection is requested.

Applicants submit that the present application is now in condition for allowance.

Early notification of such action is earnestly solicited.

Respectfully submitted,

OBLON, SPIVAK, McCLELLAND,
MAIER & NEUSTADT, L.L.P.
Stephen G. Baxter

Vincent K. Shier, Ph.D.
Registration No. 50,552

Customer Number
22850

Tel: (703) 413-3000
Fax: (703) 413-2220
(OSMMN 08/03)